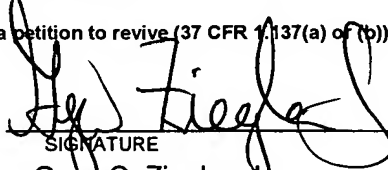


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TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A SUBMISSION UNDER 35 U.S.C. 371		ATTORNEY'S DOCKET NUMBER 785-012247-US (PAR) U.S. APPLICATION NO. (if known, see 37 CFR 1.5) <div style="font-size: 2em; font-weight: bold;">107536780</div>
INTERNATIONAL APPLICATION NO. PCT/FI2003/013468	INTERNATIONAL FILING DATE 29 NOVEMBER 2003	PRIORITY DATE CLAIMED 29 NOVEMBER 2002
TITLE OF INVENTION USE OF 2,5-DIHYDROXYBENZENESULFONIC COMPOUNDS FOR THE TREATMENT OF DISORDERS BASED ON AN IMPAIRMENT OF NO PRODUCTION AND/OR OF REGULATION OF EDHF FUNCTION		
APPLICANT(S) FOR DO/EO/US ESTEVE-SOLER, Jose, SAENZ DE TEJADA-GORMAN, Inigo, ANGULO-FRUTOS, Javier		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a submission under 35 U.S.C. 371. 2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a submission under 35 U.S.C. 371. 3. <input type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below. 4. <input checked="" type="checkbox"/> The US has been elected (Article 31). 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ol style="list-style-type: none"> a. <input checked="" type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> has been communicated by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). <ol style="list-style-type: none"> a. <input type="checkbox"/> is attached hereto. b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4). 7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ol style="list-style-type: none"> a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> have been communicated by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). 		
Items 11 to 20 below concern document(s) or information included:		
<ol style="list-style-type: none"> 11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 13. <input checked="" type="checkbox"/> A preliminary amendment. 14. <input type="checkbox"/> An Application Data Sheet under 37 CFR 1.76. 15. <input type="checkbox"/> A substitute specification. 16. <input type="checkbox"/> A power of attorney and/or change of address letter. 17. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821- 1.825. 18. <input type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 154(d)(4). 19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4). 20. <input checked="" type="checkbox"/> Other items or information: International Search Report, International Preliminary Search Report 		

This collection of information is required by 37 CFR 1.414 and 1.491-1.492. The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 15 minutes to complete, including gathering information, preparing, and submitting the completed form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

U.S. APPLICATION NO. (if known, see 37 CFR 1.5) 10/536780		INTERNATIONAL APPLICATION NO. PCT/EP2003/013468		ATTORNEY'S DOCKET NUMBER 785-012246-US (PAR)		
The following fees have been submitted				CALCULATIONS	PTO USE ONLY	
21. <input checked="" type="checkbox"/> Basic national fee..... \$300				\$ 300.00		
22. <input type="checkbox"/> Examination fee If International preliminary examination report prepared by USPTO and all claims satisfy provisions of PCT Article 33(1)-(4)..... \$100 All other situations..... \$200				\$		
23. <input type="checkbox"/> Search fee Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority..... \$100 International Search Report prepared and provided to the Office..... \$400 All other situations..... \$500				\$		
TOTAL OF 21, 22 and 23 =				\$		
<input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.						
Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof (round up to a whole number)	RATE			
X - 100 =	/50 =		x \$250	\$		
Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(h)).				\$		
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$		
Total claims	- 20 =		x \$ 50	\$		
Independent claims	- 3 =		x \$200	\$		
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				+ \$360	\$	
TOTAL OF ABOVE CALCULATIONS =				\$ 300.00		
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by 1/2.						
SUBTOTAL =				\$ 300.00		
Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(i)).				+	\$	
TOTAL NATIONAL FEE =				\$ 300.00		
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property				+	\$	
TOTAL FEES ENCLOSED =				\$ 300.00		
				Amount to be refunded:	\$	
				Amount to be charged:	\$	
<p>a. <input checked="" type="checkbox"/> A check in the amount of \$ 300.00 to cover the above fees is enclosed.</p> <p>b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. <input type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. _____. A duplicate copy of this sheet is enclosed.</p> <p>d. <input type="checkbox"/> Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.</p>						
<p>NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status.</p>						
<p>SEND ALL CORRESPONDENCE TO: Geza C. Ziegler, Jr. PERMAN & GREEN, LLP 425 Post Road Fairfield, CT 06824 203/259-1800 Customer No. 2512</p>						
				SIGNATURE 		
				NAME Geza C. Ziegler, Jr.		
				44,004		
				REGISTRATION NUMBER		

10/536780

IN THE UNITED STATES ELECTED OFFICE (EO/US)

JC13 Rec'd PCT/PTO 26 MAY 2005

REGARDING THE INTERNATIONAL
APPLICATION OF:
ESTEVE-SOLER, Jose et al.

DOCKET OR REFERENCE NUMBER:
785-012247-US (PAR)

ENTITLED:

USE OF 2,5-DIHYDROXYBENZENESULFONIC COMPOUNDS FOR THE
TREATMENT OF DISORDERS BASED ON AN IMPAIRMENT OF NO
PRODUCTION AND/OR REGULATION OF EDHF FUNCTION

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INTERNATIONAL STAGE EXPRESS MAIL CERTIFICATE

"Express Mail" label number: EV 327710470 US

Date of Deposit: 5/26/05

I hereby certify that the following attached papers and/or fee

Transmittal Letter to the United States Designated/Elected Office DO/EO/US
Front Page of WO Publication No. WO 2004/050074 A1
Preliminary Examination Report
Preliminary Amendment
International Search Report
Information Disclosure Statement/PTO1449/References Cited
Check for \$300.00
Self-addressed stamped return postcard

are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under
37 CFR 1.10 on the date indicated above and is addressed to Mail Stop PCT, Commissioner for Patents, P.O.
Box 1450, Alexandria, VA 22313-1450.

Shawna Murphy
(Typed or printed name of person mailing paper or fee)

Shawna Murphy
(Signature of person mailing paper or fee)

Each paper letter or communication relating to an international application during the international stage for which a date of filing is to be obtained as of the date of mailing must have its own certificate and the "Express Mail" label number as a part thereof or attached thereto. When, as here, the certification is presented on a separate sheet, that sheet must (1) be signed and (2) fully identify and be securely attached to the paper or fee it accompanies. Identification should include the serial number and filing date of the application as well as the type of paper being filed, e.g. complete application, specification and drawings, responses to rejection or refusal, notice of appeal, etc. If the serial number of the application is not known, the identification should include at least the name of the inventor (s) and the title of the invention.

The label number need not be placed on each page. It should, however, be placed on the first page of each separate document, such as, a new application, amendment, assignment, and transmittal letter or a fee, along with the certificate of mailing by "Express Mail". Although the label number may be on checks, such a practice is not required. In order not to deface formal drawings it is suggested that the label number be placed on the back of each formal drawing or the drawings be accompanied by a set of informal drawings on which the label number is placed.

Customer No.: 2512